

### **REMARKS**

Upon entry of this amendment claims 1-6, 12 and 23-24 will be pending in this application. Claim 12 is amended to incorporate the limitations of claim 7. Claims 7-11 and 13-22 are canceled with prejudice and Applicants reserve the right to pursue the canceled subject matter in subsequent continuing or divisional applications.

Applicants' response to the Examiner's Office Action is as follows.

#### **Claim Rejections – 35 USC §112**

The Examiner has rejected claims 7-22 under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for the in-vitro assay method, allegedly does not reasonably provide enablement for the treatment of the list of diseases or far less any disease that falls under the inhibition of NF- $\kappa$ B. According to the Examiner, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The Examiner has further requested the election of one disease for examination on the merits.

Solely in order to expedite prosecution of this application, Applicants elect the disease rheumatoid arthritis for examination on the merits. Claims 7-11 and 13-22 are canceled without prejudice, thus rendering the rejection of these claims moot. Applicants respectfully traverse the rejection of claim 12.

Applicants assert that the specification does enable one of ordinary skill in the art to use the compounds of formula (I) in the method of treating rheumatoid arthritis. At the time of filing, it was known that transcription factor NF- $\kappa$ B plays a key role in the pathogenesis of inflammatory diseases, especially rheumatoid arthritis.

Rheumatoid arthritis is characterized by inflammation and hyperplasia of the synovium. At the time of filing, it was known to one of ordinary skill in the art that NF- $\kappa$ B is highly activated in the synovium of patients with rheumatoid arthritis and could induce the transcription of proinflammatory cytokines, chemokines, adhesion molecules, and inducible nitric oxide. It was also known that NF- $\kappa$ B activation may also be a factor in protecting cells against apoptosis, thus contributing to synovial hyperplasia. (Tak et al., first paragraph, page 1897 (enclosed)). It was also known that the activation of NF- $\kappa$ B in the synovium is primarily controlled by IKK-2. Thus, the activation of NF- $\kappa$ B in the synovium can be suppressed through the inhibition of IKK-2. Given this link between IKK-2 and rheumatoid

arthritis, one of ordinary skill in the art would have considered IKK-2 a potential therapeutic target for the treatment of rheumatoid arthritis. (Tak et al., page 1906, last paragraph)

Given the recognized link between IKK-2 and rheumatoid arthritis, all one of ordinary skill in the art would need to do is test the compounds of formula (I) to determine how effectively each of these compounds is at inhibiting IKK-2. On pages 29-35 of the specification, Applicants have given several different assays that can be used to test the compounds of formula (I). Specifically, on page 30 the IKK-2 activity assay is given. One of ordinary skill in the art can use this assay to determine the level of IKK-2 inhibition each compound has. One of ordinary skill in the art can also use the assays on pages 33-35 to determine how effective the compounds of formula (I) are at treating rheumatoid arthritis in certain animal models.

Applicants assert that the specification is enabling for the method of treating rheumatoid arthritis. At the time of filing, it was known that IKK-2 inhibitors could be useful in treating rheumatoid arthritis. This knowledge coupled with the IKK-2 binding assay provided in the specification allows one of ordinary skill in the art to test the compounds of the instant invention to determine the level of inhibitory effect without undue experimentation. The animal models provided in the specification also allow one of ordinary skill in the art to test the compounds of the instant invention to determine how effective the compounds are in treating rheumatoid arthritis in animals without undue experimentation. In light of the above remarks, Applicants respectfully request that the rejection of claim 12 be reconsidered and withdrawn.

#### Allowable Subject Matter

Applicants gratefully acknowledge that the Examiner has allowed claims 1-6 and 23-24 over the prior art of record.

Conclusion

This reply is intended to further this case to allowance by addressing each ground of rejection in the Examiner's Office Action. Reconsideration of this application is respectfully requested. Authorization is hereby granted to charge any fees which may be required by this paper to Deposit Account No. 19-2570. Should the Examiner have any questions regarding this application, the Examiner is invited to call the undersigned agent at the number given below.

Respectfully submitted,

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